Claim 50 has also been amended to replace the term "comprising" with the term "consisting essentially of".

Claim 55 has been amended to exclude SEB or SEC or other native toxins. Applicants respectfully submit that the exclusion of these toxins is supported in the specification. The toxins SEB and SEC are identified in the application as being known in the art and the specific 12 mer amino acid sequences which are contained in SEB and SEC are set forth in the specification. See, e.g., page 4, lines 12-13 wherein it is stated that "the gene sequences and deduced amino acid sequences of at least six staphylococcal enterotoxins ... are known, i.e., SEA, SEB, SEC, SEE, SED and SEH." See also, e.g., page 2, line 21, p. 61, lines 18-23 and p. 63, lines 19-24 of the specification wherein the Hoffmann et al. reference (references 40 and 55 in the specification) is referred to; page 3, line 11 and p. 65, lines 15-18 of the specification where the Soos et al. reference (reference 69 in the specification) is referred to; and page 63, line 31 to page 64, line 4 of the specification wherein the Jett et al. reference (reference 58 in the specification) is referred to. See also, Figure 3 of the specification, which sets forth the specific 12-mer sequences. See also, page 24, lines 18-19 wherein it is stated that "[t]he preferred peptides of the invention are those which exclude full length native toxin molecules." See also, page 24, lines 23-25 of the specification wherein it is stated that "[t]he most preferred peptides of the invention do not contain amino acid sequences in the sequence in which they are found in any particular native toxin molecule."

Applicants respectfully submit that the above-mentioned amendments do not constitute new mater and respectfully request entry thereof.

2. The Pending Claims

Prior to entry of this amendment, claims 1-3, 7, 9, 10 and 50-59 were pending, claims 1-3, 7, 9, 10, 50-53 and 56-59 were withdrawn from consideration and claims 54 and 55, stood rejected. After entry of this amendment, claims 1-3, 7, 9, 10, and 50-59 will be pending.

3. The Restriction Requirement

The Examiner has acknowledged and entered the Amendment filed October 12, 2000, canceling claims 4-6, and 11-49 and adding new claims 50-59. The Examiner has restricted new claims 50-59 into the following groups:

- Claims 50-55 are directed to peptides (Invention I);
- Claims 56 and 57 are directed to pharmaceutical compositions (Invention II); and
- Claims 58 and 59 are directed to methods of inducing serum antibodies that bind at least one staphylococcal enterotoxin or streptococcal exotoxin, administering a peptide (Invention III).

(See, Office Action, 1/3/01, p. 2, paragraph 1).

The Examiner has acknowledged the election of Group I, claims 1-3, 50 and 51-55 and species SEQ ID NO:3 in Paper No. 8. The Examiner notes that the restriction (election) requirement in Paper No. 8 has been timely traversed. However, the requirement is still deemed proper and is therefore made final. The Examiner states that claims 54 and 55 and peptide (CMYGGVTEHEGN) will be examined in the pending application. Claims1-3, 7, 9-10, 50-53 and 56-59 have been withdrawn from consideration pursuant to 37 C.F.R. 1.142(b), as being drawn to a nonelected invention and/or species, on the grounds that there is no allowable generic or linking claim. The Examiner requests defined amino acids with sequence identifiers. (Office Action, 1/3/01, pp. 2-3, paragraphs 2-3).

Applicants reiterate that the Examiner has indicated that, upon the allowance of a generic claim, applicants will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. (Office Action, 9/12/00, p. 7). However, Applicants also note that the Examiner has indicated in the present Office Action that CMYGGVTEHEGN is considered to be generic. (Office Action, 1/3/01, p. 3). Applicants respectfully submit that a single peptide species cannot properly be considered to be generic when there are claims pending in the application with sequences that include that species, among others. Hence, Applicants respectfully request that $CMYGGX_1TX_2HX_4GN$ (SEQ ID NO: 30) of claim 50 be considered generic. Therefore, Applicants respectfully continue to traverse and request reconsideration of the restriction of at least claims 50-53 on the grounds that they are drawn to a nonelected invention and/or species, since each of the claims encompass the elected peptide species CMYGGVTEHEGN (SEQUENCE ID NO: 3), as is clear from the amended claims with the amino acid sequences written out.

The Examiner also requests defined amino acids with sequence identifiers. (Office Action, 1/3/01, pp. 2-3, paragraphs 2-3). In response, Applicants have amended claims 50 to 54 to set forth defined amino acids with sequence identifiers.

4. Inventorship

The Examiner has acknowledged the deletion of Kumar Visvanathan from the inventorship in the above-referenced nonprovisional application in view of the papers filed October 16, 2000. The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt and correction of the file jacket and PTO PALM data to reflect the inventorship as corrected. (Office Action, 1/3/01, p. 3, paragraph 4).

5. The rejection under 35 USC 112

The Examiner has rejected claims 54 and 55 under 35 USC 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter. The Examiner states that the claims should recite that it is either "isolated" or "synthetic" to insure that the claimed subject matter is not a product of nature. The Examiner also states that claims 54 and 55 depend from a nonelected claim. (Office Action, 1/3/01, p. 4, paragraph 5).

In response, Applicants have amended claim 50, from which claims 51-55 ultimately depend, to be directed to a peptide "consisting essentially of" the specified amino acid sequences. Applicants have also amended claim 55 to include the proviso that the claimed peptide is not SEB or SEC or other native toxin. Applicants respectfully submit that these amendments are sufficient to ensure that the subject matter of claims 54 and 55 are not a product of nature. Claim 54 has been rewritten in independent form. Applicants will write claim 55 in independent form upon indication of allowable subject matter if the Examiner continues to maintain the restriction requirement concerning claims 50 to 53.

6. The rejection(s) under 35 USC §§102(b)/103

The Examiner has rejected claims 54 and 55 under 35 USC §102(b) as being anticipated by Hoffman et al. (1994); Jett et al. (1994); and Soos et al. (1994). The Examiner states that the claims are directed to a peptide comprising the amino acid sequence of CMYGGVTEHEGN and that the sequence is a component of a larger molecule. The Examiner argues that Soos et al. disclose a peptide comprising the claimed amino acid sequence (Table 1, p. 598); Hoffman et al. disclose a peptide comprising the claimed amino acid sequence (Figure 5, p. 3401); and Jett et al. disclose a peptide comprising the claimed amino acid sequence (Table 1, p. 3410). The Examiner states that the prior art and the claimed invention appear to be the same or an obvious or analogous variant of the peptides claimed because they appear to possess the same or similar functional characteristics. The Examiner states that, since the PTO does not have the facilities for examining and comparing Applicants' peptide with the peptide of the prior art reference, the burden is upon Applicants to show an unobvious distinction between the material structural and functional characteristics of the claimed peptide and the peptide of the prior art. (Office Action, 1/3/01, p. 4-5, paragraph 7).

Applicants respectfully traverse the rejection. First, Applicants note that claim 50, from which claims 51-55 ultimately depend, to be directed to a peptide "consisting essentially of" the specified amino acid sequences. Applicants have also amended claim 55 to include the proviso that the claimed peptide is not SEB or SEC or other native toxin. Next, Applicants discuss each of the references in turn with respect to the elected amino acid sequence:

a. Soos et al.

Soos et al. refer to the synthesis of eight overlapping peptides spanning the entire sequence of SEB, one of which is a 38-mer synthetic peptide having the amino acid sequence: YYQCYFSKKTNDINSHQTDLRK**CMYGGVTEH*N*GN**QLDK (see, e.g., Table 1 on p. 598 emphasis added). Table 1 indicates that this peptide spans amino acid residues 90-128 of SEB. Soos et al. report testing of the peptides for binding to MHC class II molecules (see, e.g., Soos et al., abstract on p. 596 and Figure 1 on p. 598) and their ability to inhibit the mitogenic function of SEB (see, e.g., Soos et al., abstract on p. 596 and Figure 2 on p. 600). As is evident from Figure 1 of Soos et al., in contrast to other peptides, e.g., spanning regions 1-33, 31-64 and 179-212 of SEB, the peptide spanning region 90-128 of SEB was unable to displace binding of SEB to MHC containing cells (Figure 1). Furthermore, as is evident from Figure 2 of Soos et al., in contrast to the peptide spanning regions 124-154 of SEB, the peptide spanning regions 90-128 of SEB was unable to inhibit proliferation of human peripheral mononuclear cells (HPMC) by SEB.

In contrast, the present specification teaches that the 12-mer peptide 6343, having the amino acid sequence CMYGGVTEH*E*GN (SEQUENCE ID NO:3), which differs from the peptide disclosed by Soos et al. by having 22 less amino acid residues on the amino-terminal end, 1 different residue in the corresponding region, and 4 less amino acids on the C-terminal end as compared to that of Soos et al., inhibits blastogenesis of human mononuclear cell populations stimulated by SEB (see, e.g., Example 2 on pages 49-50 and Figure 7A). The specification also teaches that peptide 6348 (i.e.,**CMYGGVTEHEGN**KKNVTVQELDYKIRKYLVDNKKLYGC, SEQ ID NO:8) (emphasis added) also inhibits, albeit to a lesser extent, blastogenesis of human mononuclear cell populations stimulated by SEB (see, e.g., Example 2 on pages 49-50 and Figure

7C). The present specification also teaches that the 12-mer peptide 6343, having the sequence CMYGGVTEHEGN (SEQUENCE ID NO:3), inhibits blastogenesis of human mononuclear cell populations by SEB, SEC, SED, SPEC, SPEA and TSST-1 toxin (see Example 3 on page 50 and Figure 8) and by SPEG, SPEH, and SPEZ toxin (see Example 6 on page 53 and Figure 9).

The present specification also teaches that the 12-mer peptide 6343, having the sequence CMYGGVTEHEGN (SEQUENCE ID NO:3), binds to the MHC complex as measured by ELISA. (See, p. 15, lines 7-8, and Figure 10 (A)). Inhibition of binding of SEB toxin binding by peptide 6343 is measured by decreased anti-SEB binding at increased concentrations of added peptide 6343. (See, p. 15, lines 8-11 and Figure 10 (B)).

Finally, the present specification also teaches that the 12-mer peptide 6343, having the sequence CMYGGVTEHEGN (SEQUENCE ID NO:3), given one and two hours before administration of the toxic dose of the indicated toxin, protected 5 out of 6 mice exposed to toxin SEB; 2 out of 2 mice exposed to the toxin SPEA and 2 out of two mice exposed to the toxin TSST-1. (See Example 5 on page 52).

Thus, Soos et al. fail to disclose the specific amino acid sequence claimed by Applicants and, therefore, does not anticipate the claims under 35 U.S.C. §102. Furthermore, Soos et al. fail to teach or suggest Applicants' amino acid sequence since Soos et al. fail to provide any motivation to use an amino acid sequence having anything in common with the region of SEB spanning amino acids 90-128. In fact, Soos et al., teach away from Applicants' invention of a peptide with a sequence such as CMYGGVTEHEGN (SEQUENCE ID NO:3) having such unexpected properties such as inhibition of stimulation of blastogenesis by toxins and inhibition of binding of toxins to the MHC complex. Soos et al. also do not teach that a

peptide having the sequence CMYGGVTEHEGN (SEQUENCE ID NO:3) inhibits the toxic effects of a native toxin *in vivo*. Soos et al. is silent about whether any of the peptides disclosed therein might inhibit the toxic effects of a native toxin *in vivo*.

b. Jett et al.

Jett et al. report the synthesis of thirteen synthetic peptides, approximately 30 amino acids each, spanning the entire sequence of SEB, one of which is a 32-mer synthetic peptide having the amino acid sequence: **CMYGGVTEH*N*GN**QLDKYRSITVRVFEDGKNLL. (See, e.g., Table 1 on p. 3410 of Jett et al. (emphasis added)). This peptide spans amino acid resides 113-144 of SEB (Id.). Jett et al. tested the synthetic peptides to evaluate their effects on T-cell proliferation in a culture system containing human peripheral blood lymphocytes incubated with mononuclear cells. Four peptide regions were reported to inhibit SEB-induced proliferation; they included sequences 1 to 30 (previously thought to be involved in major histocompatibility complex class II binding), 61 to 92 (sequences which relate to the T-cell receptor site), 93 to 112 (a linear sequence corresponding to the cysteine loop), and 130 to 160 (containing a highly conserved sequence, KKKVTAQEL). (See p. 3408, abstract). Jett et al. also report that peptide 112 [sic]-144 (conjugated to KLH), showed no inhibition of SEB-induced proliferation of human peripheral blood monocytes plus lymphocytes. (See p. 3410, col. 2, 2nd full paragraph and Figure 2).

The 12-mer peptide 6343, having the sequence CMYGGVTEH*E*GN (SEQUENCE ID NO:3), which is exemplified in the present application, differs from peptide 113-144 of Jett et al. by having 1 different residue in the 12-amino acid corresponding region, and 20 less amino acids on the C-terminal end as compared to peptide 113-144 of Jett et al.

Thus, Jett et al., like Soos et al., fail to disclose, teach or suggest the unexpected properties of the peptide having the sequence CMYGGVTEH*E*GN (SEQUENCE ID NO:3), i.e., inhibition of stimulation of blastogenesis by toxins. In fact, Jett et al., teach away from this property. Jett et al. also do not teach that a peptide having the sequence CMYGGVTEHEGN (SEQUENCE ID NO:3) inhibits binding of toxins to the MHC complex or inhibits the toxic effects of a native toxin *in vivo*.

c. Hoffman et al.

Figure 5 on p. 3401 of Hoffman et al. reports four conserved regions of primary structured among sequences in the pyrogenic toxin ("PT") family including the following from a region they call "region 2":

Toxin	**Residue #**	
SEA	106	CMYGGVT*L*H*D*N*N*
SEB	113	CMYGGVTEH*N*GN
SEC1	110	CMYGG*I*T*K*HEGN
SEC2	110	CMYGG*I*T*K*HEGN
SEC3	110	CMYGG*I*T*K*HEGN
SED	101	C*T*YGGVT*P*HEGN
SEE	103	CMYGGVT*L*H*D*N*N*
SPEA	98	C*I*YGGVT*N*HEGN
SPEC	85	*YI*YGG*ITPAQN*N
TSST-1	83	*FQIS*GVT*NT*E*KL*
SEC 110-123	110	CMYGG*I*T*K*HEGN

(emphasis added).

First, Applicants note that Figure 5 in Hoffman et al. merely lists sequences. No actual 12-mer peptides corresponding to those sequences were made. Furthermore, each of these peptides differs from that elected by Applicants, i.e., CMYGGVTEHEGN (SEQUENCE ID NO:3) where indicated in italics in the sequence in the table.

In addition, Hoffman et al. report the synthesis of 12 peptides to represent section of primary sequence of the toxin SEC1. One of those peptides, designated as peptide SEC 110-123, had the sequence CMYGG*IT*K*H*EGN*HF*. (See p. 3400, cols. 1-2 and Figure 4 (B)) (emphasis added). The 12-mer peptide 6343, having the sequence CMYGGVTEHEGN (SEQUENCE ID NO:3), which is exemplified in the present application, differs from peptide 110-123 of Hoffman et al. by having 2 different residues in the 12-amino acid corresponding region, and 2 less amino acids on the C-terminal end as compared to peptide SEC 110-123 of Hoffman et al. (which corresponds to "region 2 in Figure 5 of Hoffman et al., with two additional amino acid residues at the carboxy terminal end). Hoffman et al. do not provide any experimental data indicating that SEC 110-123 might be significant. Furthermore, Hoffman et al. state that "[t]he peptides implicated in MHC class II binding in this study correspond to conserved regions 1 and 3." (See p. 3403, col. 1).

Hoffman et al. fail to dislcose, teach or suggest the unexpected properties of the peptide having the sequence CMYGGVTEHEGN (SEQUENCE ID NO:3). Hoffman et al. do not teach that a peptide having the sequence CMYGGVTEHEGN (SEQUENCE ID NO:3) inhibits binding of toxins to the MHC complex. In fact, Hoffman et al. teach that their data suggest that other regions are involved in binding of the toxin to MHC II. Hoffman et al. also do not teach or suggest that a peptide having the sequence CMYGGVTEHEGN (SEQUENCE ID NO:3) inhibits stimulation of blastogenesis by toxins and inhibits the toxic effects of a native toxin *in vivo*.

The objective standard for obviousness under 35 U.S.C. § 103 as set forth clearly by the Supreme Court of the United States in Graham v. John Deere Co., 383 U.S. 1 (1966)

requires the Examiner to ascertain: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; and (3) the differences between the claimed subject matter and the prior art. See 383 U.S. at 17. The obviousness or nonobviousness of the claimed subject matter must be determined in light of these inquiries. Moreover, the Graham Court also explained that secondary considerations such as commercial success, long felt but unsolved needs, failure of others, etc. might be utilized in determining the obviousness or nonobviousness of the invention.

The proper application of the Graham test for obviousness, as clarified by the CAFC, leads to the inescapable conclusion that the claimed peptides could not possibly have been obvious in view of the cited references. In sum, applying the proper standard for determining obviousness, the cited references do not render the claimed invention obvious.

Where a prima facie case of obviousness has not been established, an applicant is not required to conduct a comparison to "establish that there actually is a difference between the results obtained through the claimed invention and the prior art." In In re Taborsky, 183 USPQ 50, 55 (CCPA 1974), the court held that,

> [i]n determining the propriety of the Patent Office case for prima facie obviousness, it is necessary to ascertain whether the prior art teachings would appear to be sufficient to one of ordinary skill in the art to suggest making the proposed substitution or other modification. In re Lintner, 59 CCPA 1004, 1007, 458 F.2d 1013, 1016, 173 USPQ 560, 562 (1972).
>
> * * *
>
> Since we hold that the prior art of record fails to establish that the fluoro-substituted compounds recited in appellant's claims are prima facie obvious, it is unnecessary to consider any comparative evidence with respect to the properties of these compounds.
>
> In re Taborsky, 183 USPQ 50, 55 (CCPA 1974), emphasis added.

Applicants respectfully submit that, as in Taborsky, the prior art teachings are not sufficient to suggest making the claimed substitutions to one of ordinary skill in the art. The Examiner's unsupported contention that the prior art suggests the claimed peptides does not equate with a suggestion to make the specific changes that lead to the claimed peptides.

7. Prior Art Made of Record But Not Relied On By the Examiner

The Examiner refers to the following prior art made of record and not relied upon which is considered pertinent to Applicant's disclosure. The Examiner states that Iandolo et al. disclose a peptide comprising CMYGGVTLHEGN. (Office Action, 1/3/01, p. 5, paragraph 9).

8. The Information Disclosure Statement, PTO-1449 form and References

The Examiner states that the Information Disclosure Statement filed July 19, 1999 fails to comply with 37 C.F.R. 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent, each publication or that portion which caused it to be listed, and all other information that caused it to be listed. The Examiner states that it has been placed in the application file, but the information referred to therein has not been considered; and it is also noted that certain references were not found in the prior application (08/838,413). The Examiner states that these references have not been considered in this application and requests copies for review. (Office Action, 1/3/01, p. 6, paragraph 10).

Applicants respectfully submit that all the references cited in the previously filed information disclosure form(s) were submitted either in the present application or one of the prior applications. Nevertheless, Applicants are submitting herewith a supplemental information

disclosure statement (SIDS) and PTO-1449 form listing the references which the Examiner indicated had not been considered, as well as additional references. Applicants are also submitting herewith copies of each of the references referred to on the form.

9. Miscellaneous

The Examiner states that the references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record in the parent application Serial No. 08/838,413. (Office Action, 1/3/01, p. 6, paragraph 11).

CONCLUSION

Applicants respectfully submit that the instant application is in condition for allowance. Entry of the amendment and an action passing this case to issue is therefore respectfully requested. In the event that a telephone conference would facilitate examination of this application in any way, the Examiner is invited to contact the undersigned at the number provided.

Respectfully submitted,
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Dated: July 3, 2001 By

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

The claims have been amended as follows:

50. (Amended) A peptide [comprising a consensus amino acid sequence CMYGGX$_1$TX$_2$HX$_4$GN (SEQ ID NO: 30) wherein X$_1$ is selected from the group consisting of V and I; X$_2$ is selected from the group consisting of L, E, K, P and N and wherein X$_4$ is selected from the group consisting of D, N, E, Q and H] consisting essentially of an amino acid sequence selected from the group consisting of

CMYGGVTLHDGN (SEQUENCE ID NO: 32);

CMYGGVTLHNGN (SEQUENCE ID NO: 33);

CMYGGVTLHEGN (SEQUENCE ID NO: 34);

CMYGGVTLHQGN (SEQUENCE ID NO: 35);

CMYGGVTLHHGN (SEQUENCE ID NO: 36);

CMYGGVTEHDGN (SEQUENCE ID NO: 37);

CMYGGVTEHNGN (SEQUENCE ID NO: 38);

CMYGGVTEHEGN (SEQUENCE ID NO: 3); ←

CMYGGVTEHQGN (SEQUENCE ID NO: 39);

CMYGGVTEHHGN (SEQUENCE ID NO: 40);

CMYGGVTKHDGN (SEQUENCE ID NO: 41);

CMYGGVTKHNGN (SEQUENCE ID NO: 42);

CMYGGVTKHEGN (SEQUENCE ID NO: 43);

CMYGGVTKHQGN (SEQUENCE ID NO: 44);

CMYGGVTKHHGN (SEQUENCE ID NO: 45);

CMYGGVTPHDGN (SEQUENCE ID NO: 46);

CMYGGVTPHNGN (SEQUENCE ID NO: 47);

CMYGGVTPHEGN (SEQUENCE ID NO: 48);

CMYGGVTPHQGN (SEQUENCE ID NO: 49);

CMYGGVTPHHGN (SEQUENCE ID NO: 50);

CMYGGVTNHDGN (SEQUENCE ID NO: 51);

CMYGGVTNHNGN (SEQUENCE ID NO: 52);

CMYGGVTNHEGN (SEQUENCE ID NO: 53);

CMYGGVTNHQGN (SEQUENCE ID NO: 54);

CMYGGVTNHHGN (SEQUENCE ID NO: 55);

CMYGGITLHDGN (SEQUENCE ID NO: 56);

CMYGGITLHNGN (SEQUENCE ID NO: 57);

CMYGGITLHEGN (SEQUENCE ID NO: 58);

CMYGGITLHQGN (SEQUENCE ID NO: 59);

CMYGGITLHHGN (SEQUENCE ID NO: 60);

CMYGGITEHDGN (SEQUENCE ID NO: 61);

CMYGGITEHNGN (SEQUENCE ID NO: 62);

CMYGGITEHEGN (SEQUENCE ID NO: 63);

CMYGGITEHQGN (SEQUENCE ID NO: 64);

CMYGGITEHHGN (SEQUENCE ID NO: 65);

CMYGGITKHDGN (SEQUENCE ID NO: 66);

CMYGGITKHNGN (SEQUENCE ID NO: 67);

CMYGGITKHEGN (SEQUENCE ID NO: 68);

CMYGGITKHGGN (SEQUENCE ID NO: 69);

CMYGGITKHHGN (SEQUENCE ID NO: 70);

CMYGGITPHDGN (SEQUENCE ID NO: 71);

CMYGGITPHNGN (SEQUENCE ID NO: 72);

CMYGGITPHEGN (SEQUENCE ID NO: 73);

CMYGGITPHQGN (SEQUENCE ID NO: 74);

CMYGGITPHHGN (SEQUENCE ID NO: 75);

CMYGGITNHDGN (SEQUENCE ID NO: 76);

CMYGGITNHNGN (SEQUENCE ID NO: 77);

CMYGGITNHEGN (SEQUENCE ID NO: 78);

CMYGGITNHQGN (SEQUENCE ID NO: 79); and

CMYGGITNHHGN (SEQUENCE ID NO: 80).

51. (Amended) A peptide of claim 50 wherein [X_1 is V] said amino acid sequence is selected from the group consisting of

CMYGGVTLHDGN (SEQUENCE ID NO: 32);

CMYGGVTLHNGN (SEQUENCE ID NO: 33);

CMYGGVTLHEGN (SEQUENCE ID NO: 34);

CMYGGVTLHQGN (SEQUENCE ID NO: 35);

CMYGGVTLHHGN (SEQUENCE ID NO: 36);

CMYGGVTEHDGN (SEQUENCE ID NO: 37);

CMYGGVTEHNGN (SEQUENCE ID NO: 38);

CMYGGVTEHEGN (SEQUENCE ID NO: 3);

CMYGGVTEHQGN (SEQUENCE ID NO: 39);

CMYGGVTEHHGN (SEQUENCE ID NO: 40);

CMYGGVTKHDGN (SEQUENCE ID NO: 41);

CMYGGVTKHNGN (SEQUENCE ID NO: 42);

CMYGGVTKHEGN (SEQUENCE ID NO: 43);

CMYGGVTKHQGN (SEQUENCE ID NO: 44);

CMYGGVTKHHGN (SEQUENCE ID NO: 45);

CMYGGVTPHDGN (SEQUENCE ID NO: 46);

CMYGGVTPHNGN (SEQUENCE ID NO: 47);

CMYGGVTPHEGN (SEQUENCE ID NO: 48);

CMYGGVTPHQGN (SEQUENCE ID NO: 49);

CMYGGVTPHHGN (SEQUENCE ID NO: 50);

CMYGGVTNHDGN (SEQUENCE ID NO: 51);

CMYGGVTNHNGN (SEQUENCE ID NO: 52);

CMYGGVTNHEGN (SEQUENCE ID NO: 53);

CMYGGVTNHQGN (SEQUENCE ID NO: 54); and

CMYGGVTNHHGN (SEQUENCE ID NO: 55).

52. (Amended) A peptide of claim 50 wherein [X_2 is selected from the

group consisting of E or L] said amino acid sequence is selected from the group consisting of

CMYGGVTLHDGN (SEQUENCE ID NO: 32);

CMYGGVTLHNGN (SEQUENCE ID NO: 33);

CMYGGVTLHEGN (SEQUENCE ID NO: 34);

CMYGGVTLHQGN (SEQUENCE ID NO: 35);

CMYGGVTLHHGN (SEQUENCE ID NO: 36);

CMYGGVTEHDGN (SEQUENCE ID NO: 37);

CMYGGVTEHNGN (SEQUENCE ID NO: 38);

CMYGGVTEHEGN (SEQUENCE ID NO: 3);

CMYGGVTEHQGN (SEQUENCE ID NO: 39);

CMYGGVTEHHGN (SEQUENCE ID NO: 40);

CMYGGITLHDGN (SEQUENCE ID NO: 56);

CMYGGITLHNGN (SEQUENCE ID NO: 57);

CMYGGITLHEGN (SEQUENCE ID NO: 58);

CMYGGITLHQGN (SEQUENCE ID NO: 59);

CMYGGITLHHGN (SEQUENCE ID NO: 60);

CMYGGITEHDGN (SEQUENCE ID NO: 61);

CMYGGITEHNGN (SEQUENCE ID NO: 62);

CMYGGITEHEGN (SEQUENCE ID NO: 63);

CMYGGITEHQGN (SEQUENCE ID NO: 64); and

CMYGGITEHHGN (SEQUENCE ID NO: 65).

53. (Amended) A peptide of claim 50 wherein [X_4 is E] said amino acid sequence is selected from the group consisting of

CMYGGVTLHEGN (SEQUENCE ID NO: 34)

CMYGGVTEHEGN (SEQUENCE ID NO: 3);

CMYGGVTKHEGN (SEQUENCE ID NO: 43);

CMYGGVTPHEGN (SEQUENCE ID NO: 48);

CMYGGVTNHEGN (SEQUENCE ID NO: 53);

CMYGGITLHEGN (SEQUENCE ID NO: 58);

CMYGGITEHEGN (SEQUENCE ID NO: 63);

CMYGGITKHEGN (SEQUENCE ID NO: 68);

CMYGGITPHEGN (SEQUENCE ID NO: 73); and

CMYGGITNHEGN (SEQUENCE ID NO: 78).

54. (Amended) A peptide [of claim 50 wherein X_1 is V; X_2 is selected from the group consisting of E or L; and X_4 is E] consisting essentially of an amino acid sequence selected from the group consisting of CMYGGVTLHEGN (SEQUENCE ID NO: 34) and CMYGGVTEHEGN (SEQUENCE ID NO: 3).

55. (Amended) A peptide of any one of claims 50 to 54 wherein said amino acid sequence is a component of a larger molecule which is retained after dialysis to remove molecules with molecular weights of less than 6000-8000 daltons with the proviso that the larger molecule is not SEB or SEC or other native toxin.